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10/501,933	10/27/2004	Donna L. Mendrick	GENE-035/15US 071912-2115	7118

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,933	MENDRICK ET AL.	
	Examiner	Art Unit	
	LARRY D. RIGGS II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed 28 April 2008 are acknowledged and entered.

Status of Claims

Cancellation of claims 1-69 are acknowledged. Claims 70-79 are currently pending and under consideration.

Withdrawn Rejections/Objections

The objection of the disclosure in the Office action mailed 30 January 2008 is withdrawn in view of the amendments filed 28 April 2008.

The objection to claim 1 in the Office action mailed 30 January 2008 is withdrawn in view of the amendments filed 28 April 2008.

The rejection of claims 1, 3-5, 7, 9, 12-17, 20-22, 47-49, 53-56, 61 and 66 under 35 U.S.C. 112, First Paragraph, in the Office action mailed 30 January 2008 is withdrawn in view of the amendments filed 28 April 2008.

The rejection of claims 1, 3-5, 7, 9, 12-17, 20-22, 47-49, 53-56, 61 and 66 under 35 U.S.C. 112, Second Paragraph, in the Office action mailed 30 January 2008 is withdrawn in view of the amendments filed 28 April 2008.

The rejection of claims 1, 3-5, 7, 9, 12-17, 20-22, 47-49, 53-56, 61 and 66 under 35 U.S.C. 101, in the Office action mailed 30 January 2008 is withdrawn in view of the amendments filed 28 April 2008.

The rejection of claims 1, 3, 4, 9, 22, 22, 47, 61 and 66 are provisionally rejected under the judicially created doctrine of obviousness-type double

patenting as being unpatentable over claims 87-97 of copending Application 10/357507 ("App. '507"), in the Office action mailed 30 January 2008 is withdrawn in view of the terminal disclaimer approved 16 May 2008.

Terminal Disclaimer

The terminal disclaimer filed on 04/28/2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent issued from application 10/357, 507 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In *In re* Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

Claims 70-79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the specification discloses a method of creating Tables 5A-5WWW *i.e.*, obtaining Mean Tox, Mean Nontox, SD Tox, SD Nontox, and LDA Score data for particular known hepatotoxic compounds, and using the linear discriminate analysis score that measures the ability of each gene in the table to predict toxicity of a sample. Tables 5A-5WWW do not disclose expression levels, *per se*. The specification does not disclose further steps necessary for the comparison of experimental expression levels and statistical values from the database. Furthermore, Tables 5A-5WWW comprise gene GLGC IDs, the tables are over 100 pages long, and comprise GLGC IDs in random order. Further, the specification does not provide guidance how to correlate data of Tables 5A-5WWW (e.g., GLGC ID Nos.) to the data of Table 1 (SEQ ID NO, GenBank Acc. No., etc.) and to what "genes" the data from Tables 5A-5WWW correspond. Even if one could correlate the data, one would not know which GLGC ID Nos. correspond to genes and ESTs. Also, the claims, as amended, recite comparing expression levels of genes to a information in a database, wherein ten genes are selected from genes and ESTs of Tables 5A-5WWW. One would not know how to select ESTs encoding genes because, while an EST may be a small part of a gene which can be used to fish the rest of the gene out of the chromosome (see General Term: Expressed Sequence Tag at http://www.meta-library.net/bi0gloss/est-bodv.html accessed 1/17/2007), as EST is not actually a

gene. Therefore, most of the ESTs disclosed in the tables do not, in fact, comprise full sequences of genes. Moreover, in order to compare expression levels, one MUST have an "operable" sequence which can be expressed, not just its inactive part (e.g., EST). Thus, one would not know how to select 10 "genes", and therefore would not know how to compare data.

Therefore, the method of comparing gene expression levels, obtained by any randomly selected method of measurement, to data in tables 5A-5WWW in order to predict whether a compound is hepatotoxic, as in claims 70-79, is not enabled.

It is well known in the art how to measure gene expression levels; and many methods/assays for doing so are well-established. However, each method will result in different kinds of data; e.g. fluorescent vs. radioactive signals vs. colorimetric, etc. Mathematical and/or statistical manipulations of the "raw" data are required in order to make meaningful comparisons between data from different experiments. This is supported by at least the prior art of both STEINER et al. (IDS ref 461: Environ. Health Perspect. (2004) vol. 112, pp. 1236-1248) and PENNIE et al. (IDS ref 377: Toxicology in vitro (2002) vol. 16, pp. 319-326). In particular, FARR et al. (IDS ref 146: Toxicol. Sci. (1999) vol. 50, pp. 1-9) teach that data need to be normalized (p. 4) and that several genes must be included in analysis to get relevant results. The instant specification teaches that the data in the Tables is the result of statistical manipulation of data from several samples for each gene (pages 47-51). Even with normalized (for a machine or plate background) gene expression values from such fluorescent readings, a

comparison of the resulting numbers to the Tables would still be meaningless in the absence of some frame of reference. It is noted that no calculation of an LDA score, mean, (tox or nontox, or any other kind of mean) from the "measured" or test data is recited in the instant claims, such that one skilled in the art would be able to meaningfully compare the acquired gene expression data to that in the Tables.

In the absence of such steps, it would require undue experimentation for one skilled in the art to determine how to compare acquired gene expression levels to the data in the Tables in order to predict whether a compound is hepatotoxic or toxic.

Thus, claims 70-79 are rejected due to a lack of enablement.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 70-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 70 recites the limitation “differential gene expression levels for said at least ten genes upon exposure to the test compound” in lines 2-3 of step (b). The metes and bounds of differential expression are unclear. One skilled in the art would understand that a single level of expression in tissues exposed to the test compound is detected. It is unclear if the differential expression is a gene

expression compared (referenced) to a standard expression, compared to the other nine gene expressions, compared to the same gene expressed under various conditions or an expression not compared to anything.

Claim 70 recites the limitation "the normalized mean expression levels of said at least ten genes", in lines 1-2 of step (c)(ii). There is insufficient antecedent basis for the limitation. Step (b) provides for "a normalized gene expression profile of at least ten genes" in line 1. However there is no calculation of normalized mean expression levels of any of the 10 genes in the steps previously to step (c).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 70-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 60-74, 78-93, and 97 of copending Application 11/059535 ("App. '535").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 60-74, 78-93, and 97 of App. '535 encompass all elements of instant claims 70-79.

Instant claim 70 recites a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW and scoring the comparison to determine if the test compound is a hepatotoxin. Claims 71-79 depend from claim 70.

Claims 98-108 of App. '535 recite a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known

hepatotoxin/liver toxin, wherein the genes are selected from Tables 3-3DD and scoring the comparison to determine if the test compound is a hepatotoxin.

Claims 98-108 of App. '535 differs from the instant claims comparing the expression profile of the genes to a database comprising gene expression values of the genes from liver exposed to a known hepatotoxin, wherein the genes are selected from Tables 3-3DD instead of comparing expression levels of the genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW.

Clearly, claims 98-108 of App. '535 teach predicting hepatotoxicity/liver toxicity of a test compound comprising steps of preparing a gene expression profile and comparing expression levels of the genes to a database comprising mean toxic or non-toxic gene expression levels of the genes exposed to a known hepatotoxin/liver toxin and thus anticipates the instant claims 70-79.

The examiner assumes that some genes in Tables 5A-5WWW and 3-3DD overlap because both databases/models comprise genes expressed in liver tissue and are indicative of liver toxicity. It is noted that the retrieval of data from the tables is not a trivial task.

Therefore, applicants are invited to present evidence to the contrary, e.g., that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Claims 70-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7, 8, 10, 13-20 and 23-31 of copending Application 10/515,373 ("App. '373").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 1-5, 7, 8, 10, 13-20 and 23-31 of App. '373 encompass all elements of instant claims, 70-79.

Instant claim 70 recites a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW and scoring the comparison to determine if the test compound is a hepatotoxin. Claims 71-79 depend from claim 70.

Claims 1-5, 7, 8, 10, 13-20 and 23-31 of App. '373 recite a method of determining whether a compound induces at least one toxic effect comprising steps of preparing a gene expression profile from a sample exposed to a test compound and comparing the expression profile of the genes to a database comprising information from Tables 5A-5MMMMM.

Claims 1-5, 7, 8, 10, 13-20 and 23-31 of App. '373 differs from the instant claims by not using just liver samples and comparing the gene expression profile

only to mean toxic and non-toxic gene expression values but to data from Tables 5A-5MMMMM.

Clearly, claims 1-5, 7, 8, 10, 13-20 and 23-31 of App. '373 teach predicting hepatotoxicity/liver toxicity of a test compound comprising steps of preparing a gene expression profile and comparing expression levels of the genes to a database comprising mean toxic or non-toxic gene expression levels of the genes exposed to a known hepatotoxin/liver toxin and thus anticipates the instant claims 70-79.

The examiner assumes that some genes in Tables 5A-5WWW and 5A-5MMMMM overlap because both databases/models comprise genes expressed in liver tissue and are indicative of liver toxicity. It is noted that the retrieval of data from the tables is not a trivial task.

Therefore, applicants are invited to present evidence to the contrary, e.g., that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

Claims 70-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 86, 88 and 91 of copending Application 11/547,759 ("App. '759").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 86, 88 and 91 of App. '759 encompasses all elements of instant claims 70-79.

Instant claim 70 recites a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW and scoring the comparison to determine if the test compound is a hepatotoxin. Claims 71-79 depend from claim 70.

Claims 86, 88 and 91 of App. '759 recites a method of predicting at least one toxic effect of a test compound comprising steps of preparing a gene expression profile from a cell or tissue/ liver cell or tissue sample, exposed to a test compound and comparing the expression profile of the genes to a database comprising information from Tables 1, 2, 5, and 6.

Claims 86, 88 and 91 of App. '759 differs from the instant claims by comparing the gene expression profile to a database comprising quantitative gene expression information and not only to mean toxic and non-toxic gene expression values.

Clearly, claims 86, 88 and 91 of App. '759 teach predicting hepatotoxicity/liver toxicity of a test compound comprising steps of preparing a gene expression profile and comparing expression levels of the genes to a database comprising mean toxic or non-toxic gene expression levels of the

genes exposed to a known hepatotoxin/liver toxin and thus anticipates the instant claims 70-79.

The examiner assumes that some genes in Tables 5A-5WWW and Tables 1, 2, 5, and 6 overlap because both databases/models comprise genes expressed in liver tissue and are indicative of liver toxicity or toxicity. It is noted that the retrieval of data from the tables is not a trivial task.

Claims 70-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8 and 20 of copending Application 12/043,666 ("App. '666").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 8 and 20 of App. '666 encompasses all elements of instant claims 70-79.

Instant claim 70 recites a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW and scoring the comparison to determine if the test compound is a hepatotoxin. Claims 71-79 depend from claim 70.

Claim 8 of App. '666 recites a method of predicting the hepatotoxicity of a compound comprising steps of detecting the level of expression in a tissue/cell sample exposed to the compound of two or more genes from Tables 5A-5XX, wherein differential expression of the genes in Tables 5A-5XX is indicative of hepatotoxicity.

Claims 8 and 20 of App. '666 differs from the instant claims by comparing the gene expression profile to a database comprising quantitative gene expression information and not only to mean toxic and non-toxic gene expression values.

Clearly, claims 86, 88 and 91 of App. '666 teach predicting hepatotoxicity/liver toxicity of a test compound comprising steps of preparing a gene expression profile and comparing expression levels of the genes to a database comprising mean toxic or non-toxic gene expression levels of the genes exposed to a known hepatotoxin/liver toxin and thus anticipates the instant claims 70-79.

The examiner assumes that some genes in Tables 5A-5WWW and Tables 5A-5XX overlap because both databases/models comprise genes expressed in liver tissue and are indicative of liver toxicity. It is noted that the retrieval of data from the tables is not a trivial task.

Claims 70-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-46 of copending Application 12/181,020 ("App. '020").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 10 and 12 of App. '020 encompasses all elements of instant claims 70-79.

Instant claim 70 recites a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW and scoring the comparison to determine if the test compound is a hepatotoxin. Claims 71-79 depend from claim 70.

Claims 10 and 12 of App. '020 recite a method of predicting the toxic effect of a compound comprising steps of preparing gene expression profile from liver cell/tissue exposed to said compound, comparing gene expression profile to a database comprising quantitative gene expression information of genes of Tables 2 and 5 from liver cell/tissue sample that has been exposed to a toxin and quantitative gene expression information from genes of Tables 2 and 5 from a control liver cell/tissue exposed to the toxin thereby predicting a toxic effect of the test compound. Claims 11 and 13-46 depend from claims 10 and 12, respectively.

Claims 10 and 12 of App. '020 differs from the instant claims by comparing the gene expression profile to a database comprising quantitative gene

expression information and not only to mean toxic and non-toxic gene expression values.

Clearly, claims 10 and 12 of App. '020 teach predicting hepatotoxicity/liver toxicity of a test compound comprising steps of preparing a gene expression profile and comparing expression levels of the genes to a database comprising mean toxic or non-toxic gene expression levels of the genes exposed to a known hepatotoxin/liver toxin and thus anticipates the instant claims 70-79.

The examiner assumes that some genes in Tables 5A-5WWW and Tables 2 and 5 overlap because both databases/models comprise genes expressed in liver tissue and are indicative of liver toxicity. It is noted that the retrieval of data from the tables is not a trivial task.

Claims 70-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8, 20, 45-48 and 52-55 of copending Application 12/256,225 ("App. '225").

Although the conflicting claims are not identical, they are not patentably distinct from each other, because claims 8 of App. '020 encompasses all elements of instant claims 70-79.

Instant claim 70 recites a method of determining whether a test compound is a hepatotoxin comprising steps of exposing liver tissue/cells to the test compound, preparing a normalized gene expression profile from the exposed tissue/cells and comparing normalized expression profile of the toxin induced genes and normalized non-toxin induced genes to a database comprising mean

toxic and non-toxic gene expression values of genes exposed to a known hepatotoxin/liver toxin, wherein the genes are selected from Tables 5A-5WWW and scoring the comparison to determine if the test compound is a hepatotoxin. Claims 71-79 depend from claim 70.

Claim 8 of App. '225 recites a method of predicting the hepatotoxicity of a compound comprising steps of detecting the level of expression in tissue/cell sample exposed to a compound of two or more genes from Tables 1-3, wherein the differential expression of genes in Tables 1-3 is indicative of hepatotoxicity. Claims 11 and 13-46 depend from claims 10 and 12, respectively.

Claim 8 of App. '225 differs from the instant claims by comparing the gene expression profile to a database comprising gene expression information and not only to mean toxic and non-toxic gene expression values or normalized gene expression profiles.

Clearly, claim 8 of App. '225 teaches predicting hepatotoxicity/liver toxicity of a test compound comprising steps of preparing a gene expression profile and comparing expression levels of the genes to a database comprising mean toxic or non-toxic gene expression levels of the genes exposed to a known hepatotoxin/liver toxin and thus anticipates the instant claims 70-79.

The examiner assumes that some genes in Tables 5A-5WWW and Tables 1-3 overlap because both databases/models comprise genes expressed in liver tissue and are indicative of liver toxicity. It is noted that the retrieval of data from the tables is not a trivial task.

Therefore, applicants are invited to present evidence to the contrary, e.g., that the tables disclose different, non-overlapping, sets of genes, or to file a terminal disclaimer to overcome the provisional obviousness-type double patenting rejection.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Regarding applications 11/059535, 10/515373 and 11/547759, applicants argue that under MPEP §804(I)(B), if a provisional nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer.

Applicants' arguments do not overcome the rejection. A provisional nonstatutory obviousness-type double patenting (ODP) rejection is not the only rejection remaining in the earlier filed instant application. See above.

Thus, applicant is advised that until claims of the copending and/or the instant application are amended so that the claimed subject matter of the copending and the instant applications is patentably distinct, the rejection under the judicially created doctrine of double patenting will be maintained and no allowable subject matter will be indicated. A timely filed terminal disclaimer in

compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

For the reasons stated above and in the previous office action, the rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone

number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ERIC S. DEJONG/
Primary Examiner, Art Unit 1631

/LDR/
Larry D. Riggs II
Examiner, Art Unit 1631